

## **REMARKS**

### **The Amendments**

Applicants respectfully acknowledge the time and courtesy of the Examiner, Mr. Hartley, in conducting the Interview of November 7, 2003. The substance of the Interview is reflected in the above amendments and following remarks. Support for the amendments to claim 51 can be found, for example, at Example 116, which confirms the uptake of the compounds in the plaque. Furthermore, the uptake of the compounds in the plaque is depicted, for example, at figures 1, 2a and 2b.

### **The Rejection under 35 U.S.C. §103**

The rejection of claims 51-60, 82,83 and 86 over Platzek WO 97/26017 (corresponding to US 6,468,502) and the rejection of claims 51-56, 61-81, 84 and 85 over Platzek WO 99/01161 (corresponding to US 6,019,595) are respectfully traversed.

At columns 2-3 of WO 97/26017, Platzek teaches that the complexes may be used to image various tissues and that the complexes are well suited for imaging the vascular system. At columns 3-4 of WO 99/01161, Platzek teaches that the complexes are well suited for imaging the vascular system since they disperse therein after administration. Both Platzek references teach that tissues are viewed indirectly by viewing vascularization or blood flow and finding areas, which have an absence of blood flow. (See, e.g., col. 4 lines 21-38 of '959 and col. 2 lines 45-58 of '502). The references state that when their compounds are "administered into the vascular space, they are dispersed exclusively in the latter." (emphasis added); see col. 3, lines 64-67, of the '959 patent and col. 2, lines 45-48, of the '502 patent.

Neither reference teaches or suggests a method where plaque in which contrast agent

is uptaken is visualized, thereby allowing the tissue to be directly viewed rather than the mere absence of blood. It is clear from the reading of the specification as a whole, that the definition of the term "visualized" means direct visualization of tissue in which contrast agent is uptaken and that the term is used in a different sense in both cited Platzek references. There are numerous examples of applicants' manner of visualization throughout the specification. For example, on page 305-306, Examples 115 and 116, the uptake of the compounds in the plaque is confirmed. This is clearly depicted in figures 1, 2a and 2b. Furthermore, neither reference teaches or suggests a method whereby necrosis and tumors are viewed simultaneously independently from one another. (See, e.g., page 6, lines 19 to 26 of the specification, discussing the distinction of these references). Again, the references teach merely vascular imaging and, thus, cannot distinguish between differing areas which lack blood flow.

Furthermore, the uptake of contrast agent in the tissue was a previously unrecognized property. Imaging to visualize the uptake of contrast agent in tissue requires a longer waiting time than imaging the contrast agent in the prior art where the blood flow was visualized. For example, in the specification, Example 115, shows that visualization was conducted 24 and 48 hours after i.v. administration where as in col. 5, lines 30-31 of Platzek (US 6,019,959) imaging takes place directly after one-time i.v administration. The references do not suggest methods allowing for such uptake and visualizing based thereon.

Thus, the Platzek references do not teach a method of imaging in a manner so as to render the claimed invention obvious under 35 U.S.C §103. Withdrawal of the rejection on

**Terminal Disclaimer**

The requirement for a terminal disclaimer is believed to be rendered moot by the above amendments.

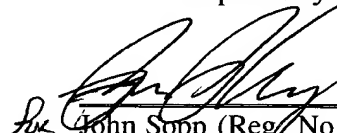
**Claim to Priority**

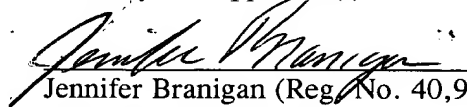
A certified copy of applicants' priority document was previously provided via hand carry and acknowledged in the Interview Summary.

It is believed that the objections and prior art rejections are overcome and the application is in condition for allowance.

Notice of the allowability of the application is requested. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

Respectfully submitted,

 (Reg. No. 32542)  
John Sopp (Reg. No. 33,103)  
Attorney for Applicant(s)

  
Jennifer Branigan (Reg. No. 40,921)  
Agent for Applicant(s)

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.  
Arlington Courthouse Plaza I  
2200 Clarendon Boulevard, Suite 1400  
Arlington, Virginia 22201  
Direct Dial: (703) 812-5305  
Facsimile No.: (703) 243-6410  
Internet Address: [jbranigan@mwzb.com](mailto:jbranigan@mwzb.com)

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